

The University of Chicago

**THE CLEAVAGE OF ETHER BY
HYDROGEN BROMIDE**

A PART OF A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
1940

By
WILLIAM B. HARDY

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The Cleavage of Ether by Hydrogen Bromide¹

BY WILLIAM B. HARDY²

This paper deals with the kinetics of the cleavage of diethyl ether by hydrogen bromide in glacial acetic acid and in several non-hydroxylic solvents. Both the order of the reaction and the effect of the alcohol formed vary with the solvent. The present results are of interest in indicating the nature of the much-discussed reverse reaction, that is, the alcoholysis of alkyl halides, when the concentration of hydroxylic reagent becomes vanishingly small. This work is the first step in an attempt to explain the direction of cleavage of unsymmetrical ethers and oxides by halogen acids.

Previous Work

So far as we have been able to determine, no kinetic studies have been made of the cleavage of ethers by a halogen acid in the absence of a hydroxylic solvent, but several studies on the reaction in glacial or aqueous acetic acid have been carried out without obtaining conclusive results. In acetic acid, the reaction is of first order with respect to ether^{3,4}; the products are an alkyl halide and an alcohol (or a phenol). In aqueous acetic acid, the reaction seems to be of second order with respect to halogen acid,⁴ but in no case has the order been definitely established. Previous work on reactions in glacial acetic acid demonstrates only that the order of the reaction depends on the ether. Tronow and Ladigina⁵ worked with a series of ethers in glacial acetic acid, used an equal concentration of hydrogen bromide in every experiment, and assumed that the reactions were all bimolecular. However, since their "constants" often increased or decreased by as much as 75% during the first half of the reaction, it may be concluded that many ethers do not cleave by a second order reaction.

Hughes and Ingold⁶ cited this work in proposing that the mechanism of cleavage depends on the structure of the ether, but their two suggested mechanisms are indistinguishable kinetically and therefore do not explain the results of Tronow and Ladigina.

The mechanism of cleavage of ethers in aqueous solution is clarified more by a study on ethylene oxides than by any study made on ethers. Brönsted, Kilpatrick and Kilpatrick⁷ showed that oxides undergo four independent reactions in dilute aqueous solution: (a) an uncatalyzed pseudo-unimolecular reaction with water to give a glycol; (b) a pseudo-unimolecular reaction (catalyzed by oxonium ion) to give a glycol; (c) a bimolecular reaction with halide ion (or any one of many other anions with the notable exceptions of perchlorate and hydroxide ions) to give a halohydrin; and (d) a trimolecular reaction with halide and oxonium ions to give a halohydrin. The well-known cleavage of ethers by aqueous halogen acids to give halides and alcohols is clearly analogous to reaction (d) of the oxides. An attempt to obtain rate constants for this ether cleavage reaction failed.⁸ Skrabal and Zahorka⁹ showed that the hydrolysis of simple dialkyl ethers with dilute aqueous sulfonic acids gives alcohols as the exclusive products and that the rate of the reaction is proportional to the first powers of the ether and acid concentrations. In this reaction (analogous to reaction (b) of the oxides), it has been impossible to determine whether, or to what extent, the solvent participates in the rate determining step, and there is little basis for choosing between the proposed mechanisms^{10,11,12} which may not differ significantly.

The hydrolysis of *cis*- and *trans*-2,3-epoxybu-

(1) Presented before the Division of Organic Chemistry at the Cincinnati Meeting of the American Chemical Society, April 9, 1940.

(2) This paper is a condensation of a portion of a thesis submitted by William B. Hardy in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Chicago. His present address is Bound Brook, N. J.

(3) Birosel, *J. Am. Chem. Soc.*, **53**, 1408 (1931).

(4) Ghaswalla and Donnan, *J. Chem. Soc.*, 1341 (1936).

(5) Tronow and Ladigina, *Ber.*, **62**, 2844 (1929).

(6) Hughes and Ingold, *J. Chem. Soc.*, 244 (1935).

(7) Brönsted, Kilpatrick and Kilpatrick, *J. Am. Chem. Soc.*, **51**, 428 (1929).

(8) Norris and Rigby, *ibid.*, **54**, 2088 (1932).

(9) Skrabal and Zahorka, *Monatsh.*, **63**, 1 (1933).

(10) Meer and Polanyi, *Z. physik. Chem.*, **19B**, 171 (1932).

(11) Bonhoeffer and Reitz, *ibid.*, **179A**, 143 (1937).

(12) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 300.

taness to glycols by means of dilute aqueous perchloric acid (reaction (b) of the oxides) has been shown to proceed with inversion and less than 10% of racemization.¹³ This result practically excludes the formation of a free radical or carbonium ion, and requires that the solvent participate in the rate-determining step. The oxide reactions (c and d) involving chloride ion are of the nucleophilic displacement type which almost invariably proceeds with inversion.¹⁴ Such evidence suggests that the cleavage of ethers in aqueous solution (at least those containing primary and secondary alkyl radicals) involves simultaneous attack of the α -carbon atom (with inversion) and the oxygen atom by the cleaving agents. The kinetic data to be presented on the cleavage of diethyl ether by hydrogen bromide strongly suggest that the same principle applies in non-aqueous solvents. This concept of simultaneous attack at two positions is supported by the recent work of Stevens.¹⁵ He reports that the cleavage of (+)-*s*-hexyl methyl ether by chloroacetyl iodide gives a secondary alcohol (ester) of the opposite configuration and suggests that reaction takes place between acetyloxonium and iodide ions.

Experimental

Preparation of Reaction Mixtures.—Two general procedures were employed for the preparation of reaction mixtures. In both, a sufficient volume was prepared and divided into several portions. After reaction, the extent of cleavage was determined by bromide titration. In experiments involving acetyl bromide, the concentration of this substance was determined by titration of an aliquot portion before the hydrogen bromide was added. The concentration of hydrogen bromide at zero time was subsequently determined by titration.

For reactions in the presence of air, aliquot samples (of about 4 cc.) were delivered from a pipet into reaction vessels which were cooled to -78° and promptly sealed. The pipet was so arranged that it could be filled by pressure from a reservoir and emptied through a 3-way stopcock with a minimum air contact and with a minimum loss of hydrogen bromide.

For reactions in the absence of air, the apparatus shown in Fig. 1 was employed. Enough stock solution (about 30 cc.) to fill six reaction tubes was introduced into the flask A. Any non-volatile component of the reaction mixture was introduced directly into C. While the bulb of A was cooled in liquid nitrogen, the remainder of the apparatus was heated with a free flame and evacuated to about 10^{-5} mm. of mercury in order to remove air and water. Stopcock B was then closed and the bulb C was

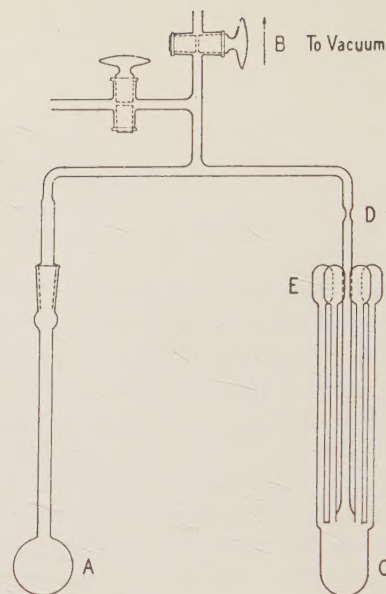


Fig. 1.—Apparatus for reactions *in vacuo*.

cooled to -80° so that the contents of A, on reaching room temperature, distilled into C. After completion of the distillation, C was cooled in liquid nitrogen, sealed off at D, and then allowed to approach room temperature. The reaction mixture in C was agitated thoroughly and then, by suitable manipulation, divided between the six reaction vessels (E). When drainage was complete, the six tubes were cooled and their necks (of 6-mm. o. d. tubing) were sealed off near the large bulb C. At this point it was found advisable to have all the necks filled to about the same height and to employ a cooling bath sufficiently deep to cover all of the liquid contents; otherwise the material in the vapor phase condensed in the six tubes in unequal proportions. The procedure described gave six reaction mixtures (one used for determination of available bromide at zero time) in which the reactants were present at equal concentrations but not in equal volumes. It was therefore necessary to weigh the contents of each reaction vessel or else to determine the volume of this vessel at several points by calibrations on its neck. After calibrations had been made, the latter procedure was more convenient. The more laborious vacuum procedure was usually employed because it eliminated the possibility of air effects, gave uniformly dry reaction mixtures, ensured the absence of high-boiling impurities, and permitted the use of concentrations of hydrogen bromide in excess of the normal solubility of this compound. The recorded runs in glacial acetic acid were carried out in the presence of air because the vacuum procedure did not give uniform reaction mixtures in this solvent.

Analyses.—When a reaction had proceeded for the required period in a thermostat, the reaction vessel after being weighed (if necessary) at room temperature, was cooled to -80° . The top of the neck was removed, and the contents were transferred (with precautions to avoid the loss of hydrogen bromide) to a flask containing water. Bromide ion in the water solution was then determined volumetrically, in order to permit the calculation of the

(13) Wilson and Lucas, *J. Am. Chem. Soc.*, **58**, 2396 (1936).

(14) For summary of evidence, see ref. (12), p. 166.

(15) Stevens, *J. Am. Chem. Soc.*, **62**, 1801 (1940).

sum of the hydrogen bromide and acetyl bromide concentrations in the reaction mixture. When both acetyl bromide and an organic liquid immiscible with water were present, vigorous and prolonged shaking was necessary to obtain complete hydrolysis of the acid halide (indicated by a permanent end-point in the titration).

Materials.—The diethyl ether was of reagent grade and was kept over sodium wire in a bottle protected from moisture. Occasional tests with ferrous and thiocyanate ions showed that the ether remained free of peroxides. Anhydrous hydrogen bromide was prepared from bromine and boiling tetralin. Approximately the desired amount of this reagent could be introduced by condensing the gas in a cooled tube and then distilling it into the cooled reaction mixture. Toluene, chlorobenzene, and chloroform were washed first with concentrated sulfuric acid and then with water; they were subsequently dried and fractionally distilled. Acetic acid and acetyl bromide were fractionally distilled. Frequently redistillation of the acid halide was necessary to obtain reproducible results. Since the use of older samples tended to make the ether cleavage too rapid, deterioration of these samples is thought to be due to atmospheric moisture.

Rate Measurements

General Statement.—This section lists the experimental determinations of the rate of cleavage of diethyl ether by hydrogen bromide to give ethyl bromide and ethanol as primary products. All the reactions except those in glacial acetic acid were carried out at 50°; acetic acid runs were made at 25°. With the exceptions noted, all of the reactions were homogeneous. Concentrations are expressed in moles per liter of solution at room temperature. In the rate equations accompanying the tables, "a" is the initial concentration of ether; "b" is the initial concentration of hydrogen bromide; "x" is the concentration of ethyl bromide (or ethanol) formed, and "t" indicates time in hours. Except as noted, rate constants are calculated from zero time.

Reasons for adding acetyl bromide to some reaction mixtures will be indicated. [Br⁻] in the tables indicates the sum of the hydrogen bromide and acetyl bromide concentrations as determined by titration in water; the ethyl bromide formed did not hydrolyze appreciably. In some experiments, duplicate determinations were made for each time interval; in most of the others, such checks were made for at least one time interval. Duplicate determinations of bromide ion seldom differed by more than 0.003 mole/liter. In view of this variation, rate constants were not calculated when the initial titration value for bromide ion had decreased by less than 0.015 mole/liter.

For reasons to be explained shortly, experiments involving acetyl bromide were seldom carried beyond 20% reaction of the ether or beyond 70% reaction of the acetyl bromide.

Reaction of Hydrogen Bromide with Excess Ether.—When anhydrous hydrogen bromide is allowed to react with excess ether, the reaction begins slowly and then accelerates, as shown by Table I. Since added alcohol similarly accelerates the reaction, the acceleration is due to the alcohol formed. Because water has an effect like that of alcohol, and because a second phase often forms after the reaction has proceeded for some time, results are not easily reproducible. The rough agreement between rate constants is further proof of the autocatalytic nature of the reaction.

TABLE I
THE REACTION OF HYDROGEN BROMIDE WITH EXCESS ETHER

Initial [HBr] = 0.573				Initial [HBr] = 0.571 Initial [EtOH] = 0.046			
t	[HBr]	k _{1a} ^a	k _{2a} ^b	t	[HBr]	k _{1a} ^c	k _{2a} ^d
1.33	0.546			1.33	0.537	0.75	1.36
4.00	.519	0.49	0.91	4.00	.459	.51	1.14
7.90	.438	.49	.96	7.90	.330	.39	1.06
13.30	.306	.34	.94	13.30	.199	.27	1.05
19.40	.188	.25	.96	19.40	.122	.18	1.09
24.67	.128	.18	.99				
Initial [HBr] = 0.698				Initial [HBr] = 0.0714			
t	[HBr]	k _{1a} ^a	k _{2a} ^b	t	[HBr]	k _{1a} ^a	k _{2a} ^b
1.25	0.671			39.50	0.0667		
2.33	.659	0.51	1.20				
5.25	.598	.51	0.78	115.0	.0555	0.26	4.23
14.75	.291	.32	.76	221.5	.0423	.12	3.12
20.50	.174	.19	.74				

^a Calculated from the equation

$$k_{1a} = \frac{2.303}{b(t_2 - t_1)} \log \frac{x_2(b - x_1)}{x_1(b - x_2)}$$

of which the differential form is $dx/dt = k_{1a}(b - x)x$. The subscript (1) refers in each case to the next preceding measurement. ^b Calculated from the equation

$$k_{2a} = \frac{1}{b(t_2 - t_1)} \left[\frac{1}{b - x_2} - \frac{1}{b - x_1} + \frac{2.303}{b} \log \frac{x_2(b - x_1)}{x_1(b - x_2)} \right]$$

of which the differential form is $dx/dt = k_{2a}(b - x)^2x$. The subscript (1) refers in each case to the first measurement after zero time. ^c Calculated from the equation (c is the initial concentration of alcohol)

$$k_{1a} = \frac{2.303}{(c + b)(t_2 - t_1)} \log \frac{(x_2 + c)(b - x_1)}{(x_1 + c)(b - x_2)}$$

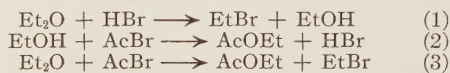
of which the differential form is $dx/dt = k_{1a}(b - x)(x + c)$. The subscript (1) refers in each case to the next preceding measurement. ^d Calculated from the equation (c is the initial concentration of alcohol)

$$k_{2a} = \frac{1}{(c + b)t} \left[\frac{1}{b - x} - \frac{1}{b} + \frac{2.303}{c + b} \log \frac{(x + c)b}{(b - x)c} \right]$$

of which the differential form is $dx/dt = k_{2a}(b - x)^2(x + c)$.

Since calculations of these constants ignore the competing uncatalyzed reaction (which is necessarily important at the beginning of an experiment), the constants in any experiment should decrease with time. For this reason, and because agreement between experiments is somewhat better for k_{1a} than for k_{2a} , the autocatalytic reaction apparently involves ether and one molecule each of hydrogen bromide and alcohol. The possibility that two molecules of hydrogen bromide, instead of one, are involved has not been excluded but seems unnecessarily complicated. It should be noted that the difficulty in deciding between k_{1a} and k_{2a} is partly due to the fact that the corresponding equations have a common term.

Use of Acetyl Bromide.—To avoid complications due to autocatalysis, separation of layers, and the resulting difficulties in reproducibility, acetyl bromide was added to many reaction mixtures to remove the alcohol formed. Reactions (1) and (2) then occurred and reaction (3) was the net result



Thus the apparent reaction is a cleavage of ether by acetyl bromide, the concentration of hydrogen bromide remaining constant. However, hydrogen bromide, not acetyl bromide, is the cleaving agent and reaction (1) is the rate-determining step because acetyl bromide does not react significantly with ether at 50° in the absence of hydrogen bromide¹⁶ and because the rate of cleavage depends on the concentration of hydrogen bromide, not (except as noted elsewhere) on the concentration of acetyl bromide.

Although the presence of acetyl bromide prevents separation of a second liquid phase and minimizes the effects of traces of water, its use introduces a complication: the ethyl acetate formed reacts with hydrogen bromide to give ethyl bromide and acetic acid. A test experiment¹⁷ showed

(16) In an 0.8 molar solution of acetyl bromide in ether at 50°, only 4% of the acid halide reacted in forty hours. The observed reaction is partly due to hydrogen bromide present in the acetyl bromide or formed by the action of traces of water.

(17) An equimolecular mixture of ether and ethyl acetate was made 0.416 molar in hydrogen bromide and allowed to react at 50°. Samples were analyzed for both hydrogen ion (consumed only in ether cleavage) and bromide ion (consumed in both ether and ester cleavage). Each set of figures represents, respectively, the elapsed time, the % of the initial hydrogen bromide reacting with ether, and the % reacting with ester: 2 hours, 5.5, 10.8; 3.4 hours, 11.8, 19.0; 20.0 hours, 47.9, 34.3; 25.2 hours, 52.9, 34.6. These data suggest that autocatalysis is more important in ether cleavage than in ester cleavage.

that ether and ethyl acetate react with hydrogen bromide at approximately the same rate. It was therefore assumed that if no more than 20% of the ether reacted in a given experiment, the effect of ethyl acetate might be neglected. This assumption is supported by the rate constants obtained both with and without solvents. Another restriction on the use of acetyl bromide is due to the fact that it is consumed during ether cleavage. Whenever the acid halide concentration dropped very much below 0.1 molar, the result of the experiment was disregarded.

Reaction of Hydrogen Bromide with Excess Ether in the Presence of Acetyl Bromide.—Table II shows that the cleavage of ether is of

TABLE II

THE REACTION OF HYDROGEN BROMIDE WITH EXCESS ETHER IN THE PRESENCE OF ACETYL BROMIDE

[HBr] ^a	[AcBr] ^b	k_2^c	[HBr]	[AcBr]	k_2
0.809	1.832	0.056	0.481	0.699	0.037
.994	1.369	.058	.481	.699	.053 ^d
.484	1.335	.057	.301	.530	.036
.392	1.217	.059	.228	.523	.040
.566	1.186	.050	.584	.349	.045
.549	1.054	.050	.173	.321	.039
.553	1.003	.052	.697	.296	.029
.530	1.003	.048	.583	.202	.026
			.486	.197	.030

^a Constant concentration of hydrogen bromide. ^b Initial concentration of acetyl bromide, decreasing as the reaction progresses. ^c Calculated from the equation $k_2 = dx/[HBr]^2 dt$ where dx/dt represents the decrease in moles per liter per hour of bromide available for titration (the sum of the constant hydrogen bromide concentration and the variable acetyl bromide concentration). ^d Acetic acid present at a concentration of 0.103 molar. The preceding experiment was carried out simultaneously as a control.

TABLE III

DATA FOR REPRESENTATIVE EXPERIMENTS IN TABLE II^a

t	[HBr] = 0.484 [Br ⁻]	k_2	t	[HBr] = 0.173 [Br ⁻]	k_2
0.0	1.819		0.0	0.494	
18.0	1.546	0.065	20.5	.479	0.036
25.2	1.494	.055	44.0	.447	.034
42.2	1.288	.054	68.0	.426	.042
49.2	1.221	.052	82.0	.390	.042
74.0	0.803	.059	109.0	.358	.042
	[HBr] = 0.697			[HBr] = 0.994	
0.0	0.993		0.0	2.363	0.058
5.0	.921	0.028	10.0	1.789	
10.58	.851	.027			
15.33	.779	.031			
21.0	.698	.029			

^a All of the values for k_2 are calculated from zero time according to the equation in Table II. The average value of k_2 for each experiment is listed in Table II.

second order with respect to hydrogen bromide when the concentration of this reagent is varied by a factor of six. Table III shows that assumptions about the function of acetyl bromide are justified by the constant rate of reaction during the period when most of the acetyl bromide was being consumed.

The experiments in Table II are arranged in order of decreasing concentration of acetyl bromide. They show that a nine-fold variation in the initial concentration of this reagent causes k_2 to vary by a factor of only two. Since the highest concentration of acetyl bromide corresponds to 225 g./liter of solution, and since acetyl bromide has a higher dielectric constant than ether, the observed phenomenon is probably a solvent effect.¹⁸ A similar effect may be noted when toluene, which has about the same dielectric constant as ether, is used as solvent. However, chloroform and acetic acid have dielectric constants which are closer to that of acetyl bromide, and in these solvents there is no noticeable effect due to variations in the initial acetyl bromide concentration.

Miscellaneous Factors Affecting Ether Cleavage.—Oxygen (air), free space in the reaction vessel, and packing this vessel with Pyrex chips were found to have little significant effect on the rate of reaction in excess ether solution.

The admission of air to runs made with acetyl bromide and prepared by the vacuum distillation procedure slightly but consistently increased the rate of reaction during the initial period; but this effect did not persist during the subsequent reaction. The first experiment in Table III, $[\text{HBr}] = 0.484$, is a representative of such runs. About half of the experiments in Table II were carried out in the absence of air; these gave better agreement between the first and subsequent values of k_2 . All of the experiments in Table I and in glacial acetic acid solution were carried out in the presence of air, but unlisted experiments showed that exclusion of air had no perceptible effect. In other solvents, experiments were usually carried out in the absence of air, but occasional duplicate runs with air failed to show any oxygen effect.

When about 4 cc. of solution was allowed to react in a vessel of 25 cc. instead of the usual 5 cc. capacity, the rate of reaction was decreased

(18) A part of the increased reaction rate in the presence of high concentrations of acetyl bromide may conceivably be due to the direct action of this compound on ether.

about 25%. The effect seems to be due to a decrease in the concentration of hydrogen bromide in the liquid phase.

The Reaction of Hydrogen Bromide with Ether in Toluene Solution.—Toluene, an inert solvent of low dielectric constant, was employed to determine the order of the ether-hydrogen bromide reaction with respect to ether. Tables IV and V show that the rate-determining step in this solvent involves two molecules of hydrogen bromide and one molecule of ether. Here, just as in excess ether, there are indications of a "solvent effect" due to acetyl bromide.

TABLE IV

THE REACTION OF HYDROGEN BROMIDE WITH ETHER IN TOLUENE SOLUTION IN THE PRESENCE OF ACETYL BROMIDE

$[\text{HBr}]^a$	$[\text{Et}_2\text{O}]^c$	$[\text{AcBr}]^b$	k_3^d
0.643	0.736	1.353	0.040
.426	.690	0.700	.026
.190	.749	.689	.020
.497	.344	.683	.022
.130	.237	.667	.023
.931	1.350	.634	.027
.612	1.683	.305	.021

^{a, b} Have the same significance as in Table II. ^c Initial concentration of ether, decreasing as the reaction progresses. ^d Calculated from the equation

$$k_3 = \frac{2.303}{[\text{HBr}]^2 t} \log \frac{a}{a-x}$$

of which the differential form is $dx/dt = k_3[\text{HBr}]^2(a-x)$.

TABLE V

DATA FOR REPRESENTATIVE EXPERIMENTS IN TABLE IV^a

$[\text{HBr}] = 0.497$			$[\text{HBr}] = 0.931$		
t	$[\text{Br}^-]$	k_3	t	$[\text{Br}^-]$	k_3
0.00	1.180		0.00	1.565	
9.50	1.166	0.018 ^b	1.75	1.510	0.026
23.50	1.134	.024	3.67	1.446	.028
33.20	1.126	.020	5.50	1.391	.028
50.00	1.102	.022	9.50	1.221	.033 ^b

^a All of the values for k_3 are calculated from zero time according to the equation in Table IV. ^b Because the reaction had taken place to too large or too small an extent, these values of k_3 were disregarded in obtaining the mean values in Table IV.

In the absence of acetyl bromide, the reaction is autocatalytic, as shown by Table VI. On the assumption that the rate-determining step involves one molecule each of ether, hydrogen bromide, and alcohol, the rate "constants" calculated agree somewhat better than those for runs in excess ether, although similar experimental difficulties were encountered.

The Reaction of Hydrogen Bromide with Ether in Chloroform Solution.—Experiments in chloro-

TABLE VI

THE AUTOCATALYTIC REACTION OF HYDROGEN BROMIDE WITH ETHER IN TOLUENE SOLUTION

Summary of experiments [HBr] ^a	[Et ₂ O] ^a	k_{2a}^b	Data for initial [HBr] = 0.422 t	[HBr]	k_{2a}^b
0.212	0.382	1.10	5.0	0.394	
.256	.361	0.95	20.2	.209	0.50
.292	.726	.87	21.7	.189	.50
.335	.863	.56	23.7	.170	.49
.422	.930	.49	26.2	.157	.45
.793	1.560	.64			

^a Initial concentrations of hydrogen bromide and ether.

^b Calculated from the equation

$$k_{2a} = \frac{2.303}{t_2 - t_1} \left[\frac{1}{b(a-b)} \log \frac{b-x_1}{b-x_2} - \frac{1}{a(a-b)} \log \frac{a-x_1}{a-x_2} + \frac{1}{ab} \log \frac{x_2}{x_1} \right]$$

of which the differential form is $dx/dt = k_{2a}(a-x)(b-x)$. The subscript (1) refers to the first measurement after zero time.

form solution were undertaken in order to test the effects of quaternary ammonium bromides (which are appreciably soluble in chloroform) on the rate of ether cleavage. The order of the reaction was found to be entirely different. Tables VII and VIII show that in chloroform, over a

TABLE VII

THE REACTION OF HYDROGEN BROMIDE WITH ETHER IN CHLOROFORM SOLUTION IN THE PRESENCE OF ACETYL BROMIDE

[HBr] ^a	[Et ₂ O] ^c	[AcBr] ^b	$k_{3/2}^d$
0.151	0.261	0.610	0.13
.304	.533	.627	.14
.455	.666	1.299	.12
.475	.673	0.357	.13
.767	.710	.710	.12
.840	.195	.606	.12
.850	1.005	.660	.13
.349	0.197	.549	.47 ^e

^{a,b,c} Have the same significance as in Table IV. ^d Calculated from the equation

$$k_{3/2} = \frac{2}{[HBr]^{3/2} t} \left[\frac{1}{(a-x)^{1/2}} - \frac{1}{a^{1/2}} \right]$$

of which the differential form is $dx/dt = k_{3/2}[HBr]^{3/2}(a-x)^{3/2}$. ^e Sufficient tetraethylammonium bromide was added to make its concentration 0.0068 molar, but only about half dissolved.

TABLE VIII

DATA FOR REPRESENTATIVE EXPERIMENTS IN TABLE VII^a

t	[HBr] = 0.304 [Br ⁻]	$k_{3/2}$	t	[HBr] = 0.850 [Br ⁻]	$k_{3/2}$
0.00	0.931		0.00	1.510	
2.00	.909	0.16	0.65	1.455	0.13
4.10	.896	.14	1.75	1.372	.12
6.00	.881	.14	2.25	1.324	.13
11.10	.842	.14	3.10	1.251	.15

^a All of the values for $k_{3/2}$ are calculated from zero time according to the equation in Table VII.

wide range of concentrations, the reaction of hydrogen bromide with ether is of three-halves order with respect to both reactants. A small proportion of tetraethylammonium bromide was found to quadruple the rate of reaction; variations in acetyl bromide concentration are of no significance.

Five (unlisted) experiments were made without acetyl bromide. Considering the usual difficulties encountered in the absence of this compound, the following conclusions seem justified. Autocatalysis is not marked and $k_{3/2}^{19}$ has the same value as in the presence of acetyl bromide. The average values over a small range of reaction are 0.26, 0.30, 0.13, 0.14, 0.17. The initial concentrations of ether and hydrogen bromide were varied by factors of seven and thirty-one, respectively.

The Reaction of Hydrogen Bromide with Ether in Chlorobenzene Solution.—In order to account for the change in reaction order in passing from toluene to chloroform solution, a few experiments were carried out in chlorobenzene which has about the same dielectric constant as chloroform. Table IX shows that in chlorobenzene solution, with acetyl bromide present, the order of the hydrogen bromide-ether reaction is the same as in toluene; the rate is about three times as great.

TABLE IX

THE REACTION OF HYDROGEN BROMIDE WITH ETHER IN CHLOROBENZENE SOLUTION IN THE PRESENCE OF ACETYL BROMIDE

[HBr] ^a	[Et ₂ O] ^c	[AcBr] ^b	$k_{3/2}^d$
0.208	0.936	0.708	0.075
.500	.558	.712	.077
.787	.260	.727	.074

^{a,b,c,d} Have the same significance as in Table IV.

The Reaction of Hydrogen Bromide with Ether in Acetic Acid Solution.—In order to include a definitely polar, ionizing solvent within the scope of this investigation, ether cleavage was carried out in glacial acetic acid solution. Because of the rapid reaction at 50°, all of the experiments in this solvent were made at 25°. Tables X and XI show that in the presence of acetyl bromide,

(19) In these experiments, hydrogen bromide as well as ether is consumed and so $k_{3/2}$ is defined by the equation

$$k_{3/2} = \frac{2}{t(a-b)^2} \left[\frac{a+b-2x}{\sqrt{(a-x)(b-x)}} - \frac{a+b}{\sqrt{ab}} \right]$$

of which the differential form is $dx/dt = k_{3/2}(a-x)^{3/2}(b-x)^{3/2}$. When $a = b$, the integrated form is

$$k_{3/2} = \frac{1}{2t} \left[\frac{1}{(a-x)^2} - \frac{1}{a^2} \right]$$

the reaction is of first order with respect to both hydrogen bromide and ether; it is independent of the acetyl bromide concentration.²⁰ Lithium bromide has only a small effect on the reaction.

TABLE X

THE REACTION OF HYDROGEN BROMIDE WITH ETHER IN ACETIC ACID SOLUTION IN THE PRESENCE OF ACETYL BROMIDE

[HBr] ^a	[Et ₂ O] ^c	[AcBr] ^b	<i>k</i> ₂ ^d
0.182	1.071	0.574	0.029
.513	0.822	.724	.025
.513	.822	.724	.018 ^e
.604	.219	.393	.027
.650	.600	1.128	.030
.766	.560	0.513	.028

^{a, b, c} Have the same significance as in Table IV. ^d Calculated from the equation

$$k_2 = \frac{2.303}{[\text{HBr}]t} \log \frac{a}{a-x}$$

of which the differential form is $dx/dt = k_2[\text{HBr}](a-x)$. Reaction temperature: 25.0°. ^e Contained lithium bromide at a concentration of 0.937 molar.

TABLE XI

DATA FOR REPRESENTATIVE EXPERIMENTS IN TABLE X

<i>t</i>	[HBr] = 0.182 [Br ⁻]	<i>k</i> ₂	<i>t</i>	[HBr] = 0.604 [Br ⁻]	<i>k</i> ₂
0.0	0.756		0.0	0.997	
16.7	.665	0.029	21.0	.932	0.028
23.7	.629	.029	28.5	.917	.027
40.5	.551	.029	51.2	.873	.027

Table XII shows that the reaction of hydrogen bromide with ether in glacial acetic acid in the absence of acetyl bromide is *retarded* by the alcohol formed, and that added water and alcohol have similar retarding effects. In the absence of added water and alcohol, the initial values of *k*₂ are about two-thirds as large as those in the presence of acetyl bromide; moreover, they decrease steadily. These low initial values of *k*₂ are probably due to the presence of water in the acetic acid used; no precautions beyond fractional distillation were taken to dry this reagent, and the acid bromide, when present, removed traces of water. The decreasing values of *k*₂ Table XII and the substantially constant values of *k*_{2b} suggest that

(20) In acetic acid solution, acetyl bromide was found to react slowly with ether in the absence of added hydrogen bromide. A solution which was 0.833 molar with respect to ether and 0.531 molar with respect to acetyl bromide lost active halogen at the nearly constant rate of 0.0020 mole/liter/hour. This slow reaction is probably due largely to free hydrogen bromide formed as follows: $\text{AcOH} + \text{AcBr} \rightleftharpoons \text{Ac}_2\text{O} + \text{HBr}$. To be entirely responsible for the reaction indicated, the hydrogen bromide concentration should have been 0.083 mole/liter. The failure of acetyl bromide to affect the rate of reaction in the experiments of Table X is apparently due to the fact that the amount of hydrogen bromide added was large compared with that which was formed from acetyl bromide and acetic acid (in the presence of hydrogen bromide).

TABLE XII

THE REACTION OF HYDROGEN BROMIDE WITH ETHER IN ACETIC ACID SOLUTION^c

Initial { [HBr] = 0.417 [Et ₂ O] = 0.719			Initial { [HBr] = 0.405 [Et ₂ O] = 0.714 [EtOH] = 0.72		
<i>t</i>	[HBr]	<i>k</i> ₂ ^a	<i>t</i>	[HBr]	<i>k</i> ₂ ^a
2.7	0.403	0.018	0.018		
19.0	.345	.015	.016	19.0	0.377
42.2	.297	.012	.016	42.2	.369
67.7	.262	.011	.016	67.7	.352
Initial { [HBr] = 0.537 [Et ₂ O] = 0.448			Initial { [HBr] = 0.512 [Et ₂ O] = 0.431 [H ₂ O] = 1.85		
13.4	0.484	0.019	0.020	122.0	0.496
36.0	.433	.015	.017		
56.0	.398	.014	.018		
96.5	.357	.012	.017		

^a *k*₂ is calculated from the equation

$$k_2 = \frac{2.303}{t(a-b)} \log \frac{b(a-x)}{a(b-x)}$$

of which the differential form is $dx/dt = k_2(a-x)(b-x)$.

^b *k*_{2b} is calculated from the equation

$$k_{2b} = \frac{2.303}{t(2a-b)} \log \frac{(a-x)b}{(b-2x)a}$$

of which the differential form is $dx/dt = k_{2b}(a-x)(b-2x)$. ^c Reaction temperature, 25°.

each molecule of alcohol formed may deprive a nearly equivalent quantity of hydrogen bromide of its ability to function in ether cleavage. That the removal of hydrogen bromide by excess alcohol or water is incomplete is shown by the rate constants obtained when these substances were added initially. If the decreases in *k*₂ are entirely due to decreases in the effective concentration of hydrogen bromide, then this effective concentration is only one-fifth the value given in Table XII in the presence of two equivalents of alcohol, one-thirtieth of the stated value in the presence of four equivalents of water.

Discussion

The experimental part of this paper has shown that three different equations are required to express the rate of cleavage of diethyl ether (to ethyl bromide and ethanol) in five organic solvents

$$d[\text{EtBr}]/dt = k_3[\text{Et}_2\text{O}][\text{HBr}]^2 \quad (4)$$

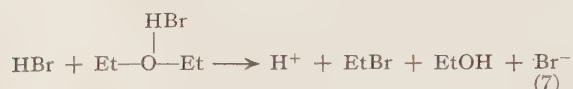
$$d[\text{EtBr}]/dt = k_{3/2}[\text{Et}_2\text{O}]^{3/2}[\text{HBr}]^{3/2} \quad (5)$$

$$d[\text{EtBr}]/dt = k_2[\text{Et}_2\text{O}][\text{HBr}] \quad (6)$$

When the catalytic effects of water and alcohol are eliminated, (4) applies to solutions in toluene chlorobenzene, and (apparently) in excess ether; (5) applies to those in chloroform, and (6) to those in glacial acetic acid.

The most probable interpretation of equation (4) is that reaction takes place between one mole-

cule of ether-hydrogen bromide complex²¹ (the concentration of which is proportional to the concentration of ether and hydrogen bromide) and a second molecule of hydrogen bromide.²² Because of the analogy with the reactions mentioned in the literature review, it is probable that the second molecule of hydrogen bromide attacks with inversion the α -carbon atom of the undissociated complex. The most obvious result is that indicated by equation (7)



In chloroform solution, equation (5) applies. Rewriting this equation as

$$d[\text{EtBr}]/dt = k_{3/2}[\text{Et}_2\text{O} \cdot \text{HBr}][\text{Et}_2\text{O} \cdot \text{HBr}]^{1/2} \quad (8)$$

shows that reaction probably takes place between one molecule of the 1:1 complex and a second substance the concentration of which is proportional to the square root of the concentration of the complex. The second substance cannot be either ether or hydrogen bromide if equations (5) and (8) are to apply; it must therefore be either a diethyloxonium ion or a bromide ion. The marked acceleration of the reaction in chloroform solution by tetraethylammonium bromide suggests strongly that bromide ion must be the active agent. It is difficult to see how this ion could assist cleavage of the complex except by attacking the α -carbon atom



The course indicated resembles mechanism (d) for oxide cleavage in the literature review. The concentration of unpaired bromide ions in chloroform solution must be very low; nevertheless comparison of rate constants shows that reaction (9) must have either a lower activation energy or a greater steric probability than reaction (7). The absence of appreciable cleavage by reaction between diethyloxonium and bromide ions (a reaction kinetically of the first order with respect to both hydrogen bromide and ether) must be due to the relative improbability of collision be-

tween two ions when both are present at very low concentrations.

The difference between the mechanisms of ether cleavage in chloroform and chlorobenzene is striking in view of the fact that both are organic chlorides with approximately the same dielectric constants (5.05 and 5.5, respectively). The hydrogen atom of chloroform is known to form hydrogen bonds with donor molecules, including ether,²³ but how the formation of a chloroform-ether complex could assist in interpreting our kinetic data is not apparent. If the chloroform assists the ionization of the ether-hydrogen bromide complex because the hydrogen of chloroform accepts a bromide ion, then the difference between ether cleavage in chloroform and in chlorobenzene (in which the hydrogen atoms do not act as acceptors) is easily explained. Bartlett and Dauben²⁴ have proposed that the hydrogen of alcohols can accept chloride ions to give hydrogen-bonded complexes.

Equation (6) expresses the rate of ether cleavage in acetic acid solution but does not permit distinction between the following possible mechanisms: (a) collision of hydrogen bromide and ether molecules; (b) slow decomposition of a 1:1 complex; (c) interaction of diethyloxonium and bromide ions; and (d) participation of the solvent in one of these rate-determining steps. We are inclined to dismiss (a) and (b) because there is no precedent for them in the other solvents, and because the reverse reaction, the alcoholysis of halides, involves when possible two or more solvent molecules.^{25,26} Possibility (c) is supported by our results in chloroform solution. This interpretation requires that the unusually rapid cleavage in glacial acetic acid be accounted for by a low concentration of dissociated ions, for even the strongest electrolytes exist partly as ion pairs in solutions much more dilute than those here employed.²⁷ If mechanism (c) is correct, the failure of lithium bromide to change markedly the rate of cleavage is due to the fact that the *product* of the concentrations of the diethyloxonium and bromide ions was unaffected. The following discussion of autocatalysis suggests that mechanism (d) is at least as satisfactory as (c).

In the absence of acetyl bromide, the rate of re-

(21) Spectroscopic evidence indicates that in non-polar solvents, such complexes are largely of the hydrogen-bonded, rather than the oxonium salt, type; cf. Buswell, Rodebush and Roy, *J. Am. Chem. Soc.*, **60**, 2528 (1938).

(22) Association of hydrogen bromide to a dimer in solution at 50° is most improbable since the pure liquid is practically unassociated at low temperatures; cf. "Gmelin's Handbuch der anorganischen Chemie," Verlag Chemie, Berlin, 8th ed., 1931, System no. 7, p. 194.

(23) Zellhoefer, Copley and Marvel, *J. Am. Chem. Soc.*, **60**, 1337 (1938).

(24) Bartlett and Dauben, *ibid.*, **62**, 1339 (1940).

(25) Farinacci and Hammett, *ibid.*, **59**, 2542 (1937).

(26) Bartlett and Nebel, *ibid.*, **62**, 1345 (1940).

(27) Kolthoff and Willman, *ibid.*, **56**, 1007 (1934).

action of hydrogen bromide with ether in toluene or excess ether solution clearly depends upon the amount of alcohol present. The data are somewhat unsatisfactory and do not permit distinction between the following rate expressions (nor exclusion of similar possibilities).

$$d[\text{EtBr}]/dt = k_{3a}[\text{Et}_2\text{O}][\text{HBr}]^2[\text{EtOH}] \quad (10)$$

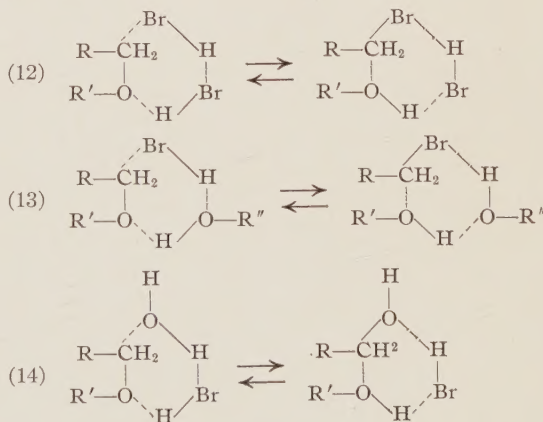
$$d[\text{EtBr}]/dt = k_{2a}[\text{Et}_2\text{O}][\text{HBr}][\text{EtOH}] \quad (11)$$

If equation (10) applies, then the effect of alcohol (or water or acetic acid which have qualitatively similar effects) may be to replace the molecule of free hydrogen bromide in equation (7) by a molecule of hydrogen bromide bound to a hydroxylic compound. Then acceleration of the reaction might be due to the fact that the proton is then set free in combination with this hydroxylic compound. If the simpler expression (11) applies, then the results indicate that one molecule of hydroxylic compound replaces one molecule of hydrogen bromide in equation (4) and in the trimolecular complex. An explanation is then apparent for the observations made for runs in acetic acid solution that the ether-hydrogen bromide reaction is of first order with respect to both reagents and also much faster than it is in any other solvent here employed: acetic acid may be one component of a trimolecular complex.

The applicability of these findings to solvolysis reactions of halides may be considered. The cleavage of diethyl ether by hydrogen bromide is the reverse of the alcoholysis of ethyl bromide. The mechanism of cleavage of ether in toluene, chlorobenzene, and excess ether solutions suggests that the alcoholysis of ethyl bromide,²⁸ when the concentration of hydroxylic molecules becomes small, should require two molecules of alcohol, or else one molecule of alcohol and a molecule of either water or hydrogen bromide.

This conclusion cannot be extended without reservations to the solvolysis of *t*-butyl²⁹ and benzhydryl halides for it has been suggested that the mechanism of halide solvolysis may change without an apparent change in the order of the reaction.³⁰ However, Farinacci and Hammett²⁵ have shown that the alcoholysis of benzhydryl chloride involves several molecules of solvent, and that water and hydrogen chloride are catalysts for this reaction. Further, Bartlett and Nebel²⁶ have

shown that the reaction of *p*-methoxybenzhydryl chloride with methanol in nitrobenzene takes place by both a bimolecular and a trimolecular process in which one or two molecules of methanol participate. Both groups of workers agree that the trimolecular reaction is only one of a series of possible polymolecular reactions. Thus, both ether cleavage and halide solvolysis under special conditions are trimolecular reactions requiring attack of the ether or halide by two molecules of reagent. Bartlett and Nebel proposed for the reaction which they studied that both molecules of methanol assist the separation of chlorine from carbon by solvating the halide ion. Regardless of whether the two attacking molecules attach themselves to one or both of the two atoms which eventually separate in the reaction, as long as the two atoms are attacked independently, ionization of some bond in the reacting complex must result, and this ionization is likely to require considerable energy under conditions where the trimolecular reaction has been observed. Manipulation of scale models, however, has shown that the trimolecular complex may assume a form containing a six-membered ring, and that cleavage of an ether or solvolysis of a halide then requires only a shift of electrons and interatomic distances, but no ionization. This scheme suggests why the trimolecular reaction may have a lower activation energy than the simpler unimolecular and bimolecular mechanisms requiring ionization. Equations (12), (13), and (14) suggest how halogen acid and hydroxylic molecules may enter into such complexes during the solvolysis of halides, the cleavage of ethers, or the etherification of alcohols



(28) Reactions involving ethylate ion are not being considered.

(29) Bartlett, *J. Am. Chem. Soc.*, **61**, 1630 (1939); Winstein, *ibid.*, **61**, 1635 (1939).

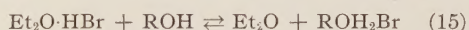
(30) Bateman, Cooper, Hughes and Ingold, *J. Chem. Soc.*, 931 (1940); Bateman and Hughes, *ibid.*, 940 (1940).

Although these formulas fix the order in which atoms must be arranged in the rings (if the reac-

tion products are specified), there is no need to specify which two molecules must combine first before the third is added. The intermediates can be constructed (with models) so that either retention or inversion (rather difficult with benzhydryl derivatives) of configuration about the α -carbon atom may occur.

The preceding discussion has suggested how water, alcohol and acetic acid may accelerate the cleavage of ether in toluene, chlorobenzene, and excess ether solutions. For chloroform solutions, no marked autocatalysis by alcohol was observed. The cleavage mechanism proposed (equation 9) does not give rise to any *additional* ions, and rearrangement of bonds apparently does not require assistance from hydroxylic molecules.

In glacial acetic acid, however, water and alcohol *retard* the cleavage of ether by hydrogen bromide. The inhibiting effects of water and alcohol can be qualitatively explained on the basis that these agents combine with hydrogen bromide according to the equation



and that the oxonium bromide formed on the right is in some cases inactive toward ether. These considerations suggest that when ether, toluene, and chlorobenzene are used as solvents, these un-ionized oxonium bromides are active agents for ether cleavage, but that the ionized oxonium bromides (either dissociated or existing as ion-pairs) in glacial acetic acid are ineffective,

like lithium bromide. The above explanation for the retarding effects of water and alcohol does not determine whether *di*-ethyloxonium ion is an intermediate in ether cleavage in glacial acetic acid and does not assist in distinguishing between the proposed mechanisms (c) and (d). The explanation requires, however, that the hydrogen bromide-acetic acid complex be substantially un-ionized in this solvent if the trimolecular complex suggested for mechanism (d) is to be retained.

Summary

The kinetics of the cleavage of diethyl ether by hydrogen bromide in ether, toluene, chlorobenzene, chloroform, and glacial acetic acid solutions have been studied. Both alcohol (formed during the reaction) and water accelerate the cleavage in ether and toluene, retard it in acetic acid, and have little effect in chloroform. In all of these solvents, the effects of water and alcohol have been eliminated by the addition of acetyl bromide to the reaction mixtures. Under such conditions the reaction is of first order with respect to ether and of second order with respect to hydrogen bromide in toluene chlorobenzene or (presumably) in excess ether; of three-halves order with respect to both reactants in chloroform; and of first order with respect to both reactants in acetic acid. The significance of these results and their bearing on the mechanism of solvolysis of alkyl halides are discussed.

